THE CONTRIBUTION OF CROSS-SENSORY ERROR SIGNALS TO REACH AFTEREFFECTS AND PROPRIOCEPTIVE RECALIBRATION

Jennifer Ruttle

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Abstract

Reaching with altered visual feedback leads to adaptation of internal motor plans, which result in aftereffects, deviated reaching without visual feedback and proprioceptive recalibration, a shift in perceived hand location (Cressman & Henriques, 2010). Zbib, Henriques, and Cressman (2016) found motor changes arise more quickly than proprioceptive changes, which required prolonged training to become significantly shifted. But their methodology may not have captured the finer incremental changes in aftereffects and proprioception. Our lab also investigated the time course of these changes using a much quicker method of proprioceptive assessment. Results suggest that both motor and proprioceptive recalibration occurred in as few as 6 rotated-cursor training trials (7.6° and 3.9° respectively). Our current study focuses on the specific contribution of cross-sensory error signals on reach aftereffects and proprioceptive recalibration. Participants moved their hand to a remembered target while they were constrained to a force channel. The cursor always moved straight to the target site, while the hand was abruptly deviated 30° CCW of the intended target (making the cursor rotation CW as per the previous study). This passive training resulted in significant aftereffects and change in felt hand position within 6 training trials. Reach aftereffects were even larger by the end of passive-training (10.6°), which were expectedly smaller than those produced during volitional reaches (15.7°). In addition, all participants recalibrated their sense of felt hand position equally (11.3°), which was larger than the shift seen with volitional reaching (5.09°). The time course of these sensory and motor

changes differed slightly across experiments but more across the different measures (motor vs. sensory). Our results suggest that proprioception is much more important for motor learning, with even the mere discrepancy between felt and seen hand location being enough to drive robust motor adaptation.

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Introduction

In order to accurately move our hands to an object, we must integrate sensory signals concerning target location and proprioceptive information regarding the arm and hands relative positions (Van Beers, Wolpert, & Haggard, 2002). Visual and proprioceptive information ordinarily correspond with each other, however, under certain circumstances, as in reaching into water, our senses do not match. When this is the case we typically rely more on vision than proprioception (Van Beers et al., 2002). These senses are used to adapt movements to continue reaching our target in the case of a mismatch. To experimentally investigate learning, motor adaptation is employed; participants must learn to modify movements in response to a perturbation, returning performance to a level seen prior to the perturbations introduction. A common experimental paradigm uses virtual reality, where the cursor representing the participants' hand is misaligned (Barkley, Salomonczyk, Cressman, & Henriques, 2014; Caithness et al., 2004; Kagerer, Contreras-Vidal, & Stelmach, 1997; Krakauer, Pine, Ghilardi, & Ghez, 2000; Neva & Henriques, 2013; Smith, Ghazizadeh, & Shadmehr, 2006; Wigmore, Tong, & Flanagan, 2002; Wong & Henriques, 2009). After training with a misaligned cursor (visuomotor adaptation) or a force field, participants have been shown to alter their hand path to ensure the cursor still reaches the target (Caithness et al., 2006). Changes in hand movements have been shown to saturate at different levels depending on whether the perturbation is introduced gradually or abruptly, with gradual introduction sometimes leading to larger aftereffects and longer retention (Kagerer et al., 1997).

Review of Literature

Goal- Directed Movement

Reaching and arm movements are executed so frequently that they are completed somewhat automatically, although still considered voluntary. Importantly, the conditions under which these reaches occur constantly change. Given the vast degrees of freedom afforded by the multi-limb interactions of reaching, our motor map encourages us to be efficient and reach straight towards our intended goal (Shadmehr & Krakauer, 2008). But these motor maps need to flexible enough to adapt to internal changes in limb length or injury as well as external perturbations of movement. In examining goal-directed movements, I will discuss the theoretical concepts, related brain areas and systems involved in adaptation and reaching control.

Theoretical Concepts of Reaching

To be able to accurately achieve our reaching goals we must have a motor plan of how to complete the movement. The brain must account for sensory inputs, goals and costs which can all be quiet variable and increase the difficulty in making efficient movements under various circumstances. Motor plans make use of and constrain this variability to create a consistent and accurate path for the end effector (Morasso, 1981). This is seen with motor equivalency when individuals make the same shape for the figure ‘8’ regardless of whether they use their hand or foot (Cisek & Kalaska, 2005). The initial position and goal are essential to creating a motor plan for goal-directed reaches, but the path must be flexible. This flexibility is accomplished by having internal models of movements that can be updated by sensory signals received during movement.

In the initial stages of movement planning the location of the target must be transformed into a compatible coordinate system for the brain to create a movement vector. This movement vector is specified in relation to the initial hand position and codes the distance and direction of movement (Krakauer, Ghilardi, & Ghez, 1999; Lalazar & Vaadia, 2008). When this vector is initially created it does not consider the joint motions required. However, this information is required to produce the correct muscle forces to account for the interaction torques created by joint motion (Krakauer et al., 1999). Creating a movement vector based solely on the goal and its location is thought to be the work of the inverse model (Kawato, 1999). Sensory feedback is used to make changes to the next action chosen. However, the sensory feedback received can be delayed by up to 300 ms and can't always be trusted (Lalazar & Vaadia, 2008). To alleviate issues associated with lag, the brain also uses predictive methods for guiding movements.

Movements are not created in isolation in the brain; many other areas receive copies of the movement trajectory. Specifically, when a movement is planned, the motor cortex sends a copy internally or 'efference copy' of the intended movement to the cerebellum and posterior parietal cortex (Desmurget & Grafton, 2000). The areas then use their prior knowledge of movement kinematics and dynamics to predict an end location (Lalazar & Vaadia, 2008). This is believed to be accomplished by the forward model. Once the movement has been completed this forward model of movement is updated based on the error between its prediction and the actual sensory consequences (Desmurget & Grafton, 2000). Forward models can update movements faster than inverse models, but both have been shown to be integral to motor learning.

Reaching Brain Areas

The brain areas involved in voluntary reaches have been most extensively researched in non-human primates. However, many homologs in the human brain have also been uncovered and will be the main focus of this section. The brain regions of particular importance for goal-directed reaching and motor adaptation are: parietal cortex; premotor areas (ventral premotor area (PMv) and dorsal premotor area (PMd), the primary motor area (M1), supplementary motor area (SMA); basal ganglia and the cerebellum.

The posterior parietal cortex integrates multisensory information to create a movement vector in eye, head, body, and world centered reference frames (Kalaska, Scott, Cisek, & Sergio, 1997). The areas directly involved in this transformation are the medial wall of the sulcus, more specifically the medial intraparietal cortex and the medial surface of the hemisphere, area 7 and the medial dorsal parietal cortex. Visual and somatosensory information regarding the current state of the limbs is received and then used for state estimation, a vital component required for certain reference frames (Fogassi & Luppino, 2005; Shadmehr & Krakauer, 2008). Subregions of the parietal cortex have been shown to use different inputs to complete similar goals; i.e. vector creation and state estimation. A double dissociation task conducted with non-human primates found damage to the superior parietal lobule impacted reaches made in the dark but not in the light, indicating this area receives proprioceptive information (Rushworth, Nixon, & Passingham, 1997). In contrast, lesions to the inferior parietal lobule impaired reaches made in the light but not in the dark, meaning this area may rely more heavily on vision (Rushworth et al., 1997). A lot of what is known about the

parietal cortices involvement in movement comes from patients with lesions to this area of the brain.

A disorder of particular interest is optic ataxia, which is a lack of coordination between visual inputs and hand movements. Optic ataxia stems from lesions in the medial occipito-parietal junction (mOPJ), the superior occipital gyrus, the intraparietal sulcus and either the superior parietal lobule or the inferior parietal lobule (Culham & Valyear, 2006; Karnath & Perenin, 2005). These patients have difficulty reaching especially when targets are in the periphery. The mOPJ has been highly implicated in decoupling eye-hand coordination which is why these patients tend to reach where they are looking even if that isn't the intended target location (Culham & Valyear, 2006). Healthy controls can also be made to do this behaviour by applying transcranial magnetic stimulation (TMS) to the posterior parietal cortex (van Donkelaar & Adams, 2005). It is clear that in regards to reaching, the parietal cortex is crucial for encoding the target and reaching hands location.

The premotor and primary motor cortex receive inputs from many locations within the brain including but not limited to: medial intraparietal cortex, medial dorsal parietal cortex and the parieto-occipital cortex (Kalaska et al., 1997). The premotor cortex is subdivided into the ventral (PMv) and dorsal (PMd) premotor cortex. The PMv may be involved in transforming coordinates from extrinsic (world) to intrinsic reference frames (hand or eye) to guide movements. This may be accomplished by signaling the location of visual stimuli relative to the body through the cells' somatic receptive field, which are immediately adjacent to each other (Graziano, Hu, & Gross, 1997). Whereas the PMd encodes the context-dependent selection and planning of movements specifically in

conditions that involve arbitrary stimulus-response pairings (Boussaoud & Wise, 1993; Hoshi & Tanji, 2006; Kalaska et al., 1997; Shen & Alexander, 1997). Both the PMv and PMd project to the primary motor cortex (M1) where the behavioural response output is generated (Kalaska et al., 1997; Zhang, Riehle, Requin, & Kornblum, 1997). M1 must encode movement trajectories in limb or body centered co-ordinates as it sends a signal to the spinal cord to specify the required limb movements (Kalaska et al., 1997; Zhang et al., 1997). There seems to be a gradient of activity present during motor movements, with activity beginning in the parietal cortex and migrating to the premotor and primary motor cortices. This occurs as the target-related computation declines and limb-movement specificity becomes more important (Kalaska et al., 1997).

The brain areas described above are necessary for the production of a movement but when a perturbation is experienced additional brain areas are recruited. These brain areas are involved in the updating and consolidation of movements during motor learning. The basal ganglia (BG) are essential for selection and inhibition of movements. The BG send projections through the thalamus to the premotor and primary motor cortices as well as the prefrontal, temporal and parietal cortex (Doya, 2000). It has many similar connections as the cerebellum but has very different synaptic mechanisms at play within its circuits. The projections and dopaminergic fibers within the substantia nigra make the BG well suited for reinforcement learning. The BG evaluates the current situations reward and selects the appropriate action based on this perceived reward.

The brain area most often attributed to motor learning and adaptation is of course the cerebellum. The cerebellum has been extensively examined through patient studies

and more recently by using transcranial magnetic stimulation (TMS) or transcranial direct current stimulation (tDCS) to either increase or decrease activation. It receives projections from the spinal cord, inferior olivary nucleus, vestibular nuclei and the pons. The main output of the cerebellum is the Purkinje cell which predominantly projects to the deep cerebellar nuclei. This neuron dense part of the brain controls equilibrium, posture, muscle tone and coordinates movement. The cerebellums input led researchers to believe it may house the forward model of movement. This is because it appears to compare the predicted sensory consequences of an action (based off of the efference copy received from M1) to the actual consequences of that movement (Desmurget & Grafton, 2000; Galea, Vazquez, Pasricha, Xivry, & Celnik, 2011; Yavari et al., 2016).

This link between the forward model and the cerebellum has been supported by studying patients with damage to this brain region. Generally, all individuals demonstrate an inability to perform certain movements, lack coordination and exhibit poorer accuracy when moving (Bastian, Martin, Keating, & Thach, 1996; Kelly & Shanley, 2016; Therrien, Wolpert, & Bastian, 2016; Werner, Bock, & Timmann, 2009). Recent studies have shown that the particular deficits in adaptation one experiences heavily depends on the location and degree of damage (Burciu et al., 2014; Kelly & Shanley, 2016; Rabe et al., 2009; Werner, Bock, Gizewski, Schoch, & Timmann, 2010). Patients with ischemic lesions in the area of the superior cerebellar artery (SCA) are the most impaired at adaptation (Henriques, Filippopulos, Straube, & Eggert, 2014; Rabe et al., 2009; Werner et al., 2010). Similar lesions to the anterior inferior cerebellar artery (AICA) and the posterior inferior cerebellar artery (PICA) have also been shown to

cause impairment to visuomotor rotations. However, their performance is much more similar to controls than SCA lesion patients (Henriques et al., 2014). The deficits seen in cerebellum patients indicate its prominent role in error based motor learning.

State Estimation

The brain needs to know where the limbs are with respect to the body to make reaches. State estimation which uses sensory signals from vision and proprioception is used to identify the location of the end-effector (Sober & Sabes, 2003, 2005; Van Beers, Sittig, & Denier Van Der Gon, 1999). Proprioception provides information regarding where an individual's limbs are with respect to other limbs and the trunk of the body (Yousif, Cole, Rothwell, & Diedrichsen, 2015). Proprioception has been divided into at least two subtypes: static and dynamic (Fuentes & Bastian, 2010). Static proprioception involves sensing the limb's position while it is stationary (Yousif et al., 2015). Dynamic proprioception involves estimations of limb position and velocity during an active reach or during passive placement. The proprioceptive signals arise from four main mechanoreceptors: muscle spindles, Golgi tendon organs, receptors in the joint capsules and stretch-sensitive receptors in the skin (Yousif et al., 2015). Muscle spindles, which are innervated by large myelinated primary afferent fibers (Aa), signal the length and rate of change in the muscle (Edin & Vallbo, 1990; Gilman, 2002). The golgi tendon organs respond to muscle tension and are innervated by large myelinated 1b and Aa fibers (Prochazka & Wand, 1980). The final two signals play a much more minor role and are innervated by small and large myelinated fibers (Aimonetti, Hospod, Roll, & Ribot-Ciscar, 2007). Together these sensory signals combine to create a proprioceptive estimate of limb location.

Proprioceptive signals are integrated with vision and weighted based on the quality of the signal. Proprioception is weighted more heavily than vision when the hand is actively moved or vision is degraded (Shi & Buneo, 2011). This is also true when moving in the depth direction; whereas vision is more heavily weighted in the azimuth direction (Van Beers et al., 2002). However, there is a 100-300 ms delay in visual feedback, making it inefficient for updating movements (Desmurget & Grafton, 2000). To improve estimates the brain also uses efference copies to generate a prediction of movements and compare that with the actually sensory consequences (Desouza, Dukelow, Gati, Menon, & Andersen, 2000; Miall, Christensen, Cain, & Stanley, 2007). These predictions are incredibly important for making quick movements and reacting to unexpected perturbations. With state estimation being an iterative process the brain continually updates the estimate of location. Prediction and sensory feedback are involved in state estimation just as they are in motor adaptation.

Motor Adaptation

Motor adaptation involves updating movements to account for internal and external changes. Examples of these changes are our limbs growing and changing strength or when we use a different type of baseball bat. Ideally, motor adaptation allows performance to return to a baseline level even in the face of limb change or novel tool use. The original internal model of movement is updated using the error between actual and expected motor outcomes. This updating returns performance to its original state and may become the new default model of movement depending on factors that will be discussed later.

In the lab, motor adaptation can be elicited by perturbing the movement kinematics by altering visual feedback of the hand (visuomotor adaptation) or perturbing the dynamics by an applied force on the hand or arm during movement. The typical motor adaptation paradigm involves participants reaching to visual targets, a cursor represents their hand location. The perturbation is then introduced and in the case of visuomotor adaptation, the motion of the hand-cursor is rotated or translated away from that of the unseen hand. In the case of a dynamic force-field perturbation, systematic forces are applied the participant's hand which is deflected away, usually in the orthogonal direction, from their intended hand path. A velocity-dependent force field involves imposing forces that are at a maximum at the point of peak velocity. In response to either type of novel perturbation, participants initially make large reach errors, but quickly modify their reaching movement in response to the perturbation and return to baseline performance. Krakauer et al., (2000) found that the learning rate of an abruptly rotated cursor is quite quick, with participants modifying their reaches back to baseline levels within 20 trials for a single target. When the targets were more numerous and spread apart radially, the number of trials increased to about 60 (Krakauer et al., 2000; Mcdougle, Bond, & Taylor, 2015). When reach targets are presented near each other, the learning accumulating at one target is generalized to nearby targets (Krakauer et al., 2000; Mcdougle et al., 2015). Generalization can increase the speed of learning when actions are repeated to the same area of the workspace.

Measures of Motor Learning

The degree to which individuals can adapt to kinematic and dynamic perturbations has been studied by measuring generalization, savings or interference and reach aftereffects. Generalization is a process by which learning to one area of the workspace translates to a novel target location. Learning generalizes best to near and far distances but substantially less for different movement directions (Ghilardi, Gordon, & Ghez, 1995; Krakauer et al., 2000; Mostafa, Kamran-Disfani, Bahari-Kashani, Cressman, & Henriques, 2014; Poggio & Bizzi, 2004). Savings is characterized by improved performance when relearning the same rotation later. Savings can be seen up to a week after the initial training (Caithness et al., 2004; Krakauer & Shadmehr, 2006), Yamamoto, Hoffman, and Strick, (2006) used a joystick paradigm and savings was present even a year later.

Another common measure of adaptation is reach aftereffects; when the perturbation is suddenly removed participants still make deviated reaches, as they were during training (Shadmehr & Mussa-Ivaldi, 1994). Following training with a kinematic or dynamic perturbation, aftereffects are shown to be approximately 50-80% of the imposed distortion, regardless of rotation direction, duration of training or cursor feedback as well as size of rotation (Barkley et al., 2014; Criscimagna-Hemminger, Bastian, & Shadmehr, 2010; Neva & Henriques, 2013; Ruttle, Cressman, ’t Hart, & Henriques, 2016; Salomonczyk, Cressman, & Henriques, 2011; Shadmehr & Brashers-Krug, 1997; Shadmehr & Mussa-Ivaldi, 1994; Wong & Henriques, 2009). Aftereffects are not only robust immediately following classic training but also remain 24 hours later (Caithness et al., 2004; Nourouzpour, Salomonczyk, Cressman, & Henriques, 2014).

Aftereffects are believed to be the evidence of an updated forward or inverse model and are only present when deep motor learning has occurred.

Proprioceptive Recalibration

Proprioception plays a role in state estimation and motor learning, thus how the estimates produced alter throughout training also requires discussion. There are many ways in which proprioception of the hand can be measured. Participants can simply point to their unseen target hand with the opposite hand (Block & Bastian, 2010; 2011) or indicate the distance the arm was moved (Bhanpuri, Okamura, & Bastian, 2013). Another perceptual task has participants report if their robot-led hand felt left or right of a reference marker (Mattar, Darainy, & Ostry, 2013; Mostafa, Salomonczyk, Cressman, & Henriques, 2014; Ostry, Darainy, Mattar, Wong, & Gribble, 2010; Salomonczyk et al., 2011). This is referred to as a two alternate-force choice task (2-AFC), as participants had to choose one of two answers (left or right). There was no visual feedback provided and participants made no volitional hand movements. Another method used, hereby referred to as a proprioceptive localization, involved participants indicating on a touchscreen or with a computer mouse where they believed their unseen adapted hand was moved to (’t Hart & Henriques, 2016; Clayton, Cressman, & Henriques, 2014; Izawa, Criscimagna-Hemminger, & Shadmehr, 2012; Ruttle et al., 2016; Yousif et al., 2015).

Using the methods described above, it has been shown that adaptation to visual and dynamic perturbations also leads to a shift in proprioceptive estimates of the trained hand’s position. This is believed to occur because vision dominates proprioception and

causes the felt hand position to shift (recalibrate) to be more consistent with the previously experienced vision of the hand (the cursor location). This recalibration is usually 20-30% of the distortion and occurs regardless of whether the distortion is a rotation or a lateral displacement, how the hand is moved during proprioceptive testing and the magnitude of the rotation (Barkley et al., 2014; Cressman & Henriques, 2010; Ruttle et al., 2016; Salomonczyk et al., 2011). This proprioceptive recalibration also remains 24 hours later (Nourouzpour et al., 2014). A similar change in felt hand direction was found following adaptation to a force field (Mattar et al., 2013; Ostry et al., 2010). Ostry et al., (2010) found that as little as ten minutes of force field training caused a perceptual change which was still present 24 hours later. In summary, following perturbed training proprioceptive recalibration is robust and ubiquitous with motor adaptation, as are reach aftereffects.

Error Signals in Motor Learning

Motor learning is driven by signals received by the central nervous system, which are used to change future performance. There are many sources of these signals but here I focus on those generated by errors in performance or error based learning. Under the umbrella of error based learning is sensory error prediction which is comprised of the cross-sensory and sensorimotor error signal. The unseen trained hand is usually represented by a cursor which is deviated with respect to actual hand movements. This mismatch between actual and visually perceived hand location causes a visual-proprioceptive mismatch or the cross-sensory error signal. In addition, as participant's move their hand there is a discrepancy between actual and desired movement

outcome, this is the sensorimotor error signal. Both of these signals are used to update internal models and future reach trajectories.

Taylor, Krakauer, and Ivry, (2014) built on this idea of sensory prediction errors updating the forward model, which they believed to be primarily an implicit process. They required half their participants to indicate where they were planning to aim before each 45° rotated training trial. They then subtracted this intended aiming angle (measure of explicit learning) from the actual aiming angle to give them a measure of implicit learning. Their results led them to believe that implicit and explicit learning evolved separately, with implicit learning being driven by sensory prediction errors whereas explicit learning is being modulated by target error (Taylor et al., 2014). Other studies from various laboratories have agreed with this conclusion, that explicit and implicit processes are separate processes, that both drive motor learning (Benson, Anguera, & Seidler, 2011; Taylor, Klemfuss, & Ivry, 2010) .

Size of Error Signal

There is some disagreement over how abrupt perturbations or large errors versus gradual distortions or small errors impact learning. Kagerer et al., (1997) found that participants who learned a gradual visuomotor rotation were less variable and had larger aftereffects. Saijo & Gomi, (2010) also found that when a rotation of 60° was introduced gradually, aftereffects were larger without increasing reaction times. They concluded that the increase in reaction time following the abrupt rotation allowed for the involvement of explicit processes (Saijo & Gomi, 2010). Further evidence for a separation between gradual and abrupt perturbations comes from Schlerf, Galea,

Bastian, and Celnik, (2012) who found that the cerebellum decreases its overall level of inhibition during early learning of an abrupt perturbation. This was not the case during the gradual perturbation condition. Werner, Schorn, Bock, Theysohn, and Timmann, (2014) also found the basal ganglia are more active during an abrupt rotation than gradual. In contrast, Buch, Young, & Contreras-Vidal, (2003) found no difference in aftereffects in their control group when training with a 90° rotation. They also included older adults in their study and found that a gradual rotation produced more complete learning than the abrupt condition for that specific group (Buch et al., 2003). . Taken together, it appears that an abrupt rotation may be more explicit and produce quantitatively different learning than that of a gradual rotation, which could involve more implicit learning. To better understand the changes seen in motor and sensory systems, they must be investigated throughout training and not just at the completion. This would allow us to identify if motor and sensory changes follow the same time course.

Time Course of Motor Learning

Many laboratories have tried to model motor learning; from aspects as simple as the process by which movements are produced, to how they are updated throughout training. Smith et al., (2006) investigated multiple models and their ability to fit the reach adaptation data and found that a multi-rate model provided the best fit. Specifically, they found that a two-rate model with a fast process and a slow process was superior. The fast process is sensitive to the large errors experienced at the beginning of training and quickly learns to counter the perturbation. It also quickly forgets what it has learned and becomes a less prominent force in adaptation. The slow process compliments the fast

process by learning much slower but also retaining this new mapping for much longer. This model was originally tested on a force field paradigm.

Mcdougle, Bond, and Taylor, (2015) recently replicated the Smith et al., (2006) study with a visuomotor rotation, believing that implicit and explicit learning would map onto the slow and fast process respectively. They also required participants to indicate where they planned to aim before each rotated training trial, to be able to characterize the implicit and explicit contributions. They concluded that the time course of implicit learning was similar to the slow process, while the explicit learning reflected the fast processes contribution to motor output (Mcdougle et al., 2015). It seems that sensory prediction errors lead to an updating of forward models and contribute to implicit learning, whereas reward prediction errors and explicit learning leads to changes in the inverse model (Izawa & Shadmehr, 2011). Thus, implicit and explicit learning processes have been shown to inform each other. However, their exact contributions to motor learning in general are still not fully understood (Taylor & Ivry, 2012).

Recently, a few labs have begun measuring these sensory and motor changes during training (Mattar et al., 2013; Zbib et al., 2016). However, they still included large chunks of training before measuring either aftereffects or proprioception. Mattar et al., (2013) looked at the evolution of learning during a force field perturbation and found that proprioception gradually shifted throughout training, requiring ~76 trials to become significantly shifted from baseline. This finding was supported by Zbib et al., (2016) using a visuomotor paradigm. They also found that proprioception slowly shifted and requiring at least ~70 rotated training trials. However, one drawback to these studies was the method of proprioceptive measurement. Both studies used a 2-AFC task where

the subjects indicated if their hand had been moved to the right or left of a reference marker. After each measurement of proprioception when subjects returned to training there was clear evidence of relearning. A study by our lab, Ruttle et al., (2016) also investigated the time course of motor learning, but measured aftereffects and proprioception every 6 rotated training trials. We did this by using a quicker and potentially more sensitive task for measuring proprioception, the proprioceptive localization task discussed above. Ruttle et al., (2016) found that within only 6 rotated training trials, both sensory and motor shifts were significant, almost reaching asymptote. While those results highlight the speed at which these changes take place, the reach aftereffects were likely still the result of a different process as compared to the proprioceptive recalibration.

While the extent of aftereffects and proprioceptive changes during classic visuomotor training are known. Little is known about the time course of motor and sensory changes and the specific error signals that drive this adaptation. Classic visuomotor training allows the participant to freely move their right hand towards each target. This enables the motor system to send an efference copy of the intended movement to the cerebellum to produce an estimate of the expected or predicted outcome, which in turn is compared to the actual consequences of the movement. This discrepancy is the sensorimotor error signal, which is then used to update and modify the computations necessary to move the end effector closer to the target. At the same time, the hand holding the robot is felt to be in a different location than the cursor displayed on the screen. This visual-proprioceptive mismatch is the cross-sensory error signal. During classic visuomotor training, both error signals are available to the brain to

update movements. Since it is difficult to remove this proprioceptive mismatch, our lab developed a reach training paradigm that removed the sensorimotor error signal. This was accomplished by restricting hand movements in the radial direction. The cursor always moves directly to the target with the hand being restrained to a force channel. This reduces any experienced discrepancy between actual and desired movement, but spares the proprioceptive mismatch between hand and cursor. The participants are essentially exposed to the altered visual feedback of the hand without the ability to explore the perturbation and how to counteract it. We call this type of training, exposure training, and believe it allows us to investigate the influence of the cross-sensory error signal on the time course of motor learning and proprioceptive recalibration.

Our lab has previously used the exposure training paradigm with a gradually rotated cursor, the force channel was gradually rotated .75° every trial until it reached the full rotation. In contrast to classic visuomotor training, exposure training created reach aftereffects of only ~7° and a shift in felt hand position of ~5.5°. In addition, increasing the size of the rotation did not increase the size of aftereffects or proprioceptive recalibration (Cressman & Henriques, 2010; Salomonczyk, Cressman, & Henriques, 2013). It is clear that even with the reduction in available error signals, the central nervous system still learns from the imposed rotations and causes a shift in internal models.

There is no information on the time course of learning when only a cross-sensory error signal is available. To be able to fully appreciate proprioception's contribution to motor learning, we must understand how the time course of motor learning varies from classic to exposure training. Here we set out to measure just that, the time course of

aftereffects and proprioceptive recalibration when only a discrepancy between proprioceptive and visual estimates of hand location can evoke adaptation.

Hypothesis

The paradigm used in this experiment should allow us to identify proprioception's contributions to motor learning and aftereffects. By not allowing participants to volitionally reach we only allow them to use the proprioceptive error signal to update their internal models of movement. Meaning the mechanism responsible for both motor and sensory changes should be the same, cross-sensory error. We expect to also see slightly smaller reach aftereffects; however sense of felt hand position should shift to the same degree as during traditional volitional cursor training. I believe that this pattern of results arise as exposure training may rely more heavily on proprioception than on vision alone.

Methods

Participants

The experiment included 39 (mean age = 23.6, range =18-47, males = 13) right-handed, healthy adults. Participants were naïve to the purpose of the study and were given course credit for participation. All participants had normal or corrected to normal vision and were free from any physical or neurological conditions. All participants provided written informed consent and the study was conducted with approval and in accordance with the ethical guidelines set by the York Human Participants Review Subcommittee.

Apparatus

A view of the experimental set-up is provided in Figure 1. Participants sat in a chair that could be adjusted with respect to height and distance from the display so that they could comfortably see and reach to each of the target locations presented on a reflective screen (Fig 1A). With their right hand, participants held onto a vertical handle on a two-joint robot manipulandum (Interactive Motion Technologies Inc., Cambridge, Ma, USA) such that their thumb rested on top of the modified handle. The reflective screen was mounted on a horizontal plane 18 cm above the two-joint robotic arm. Visual stimuli were projected from a monitor (Samsung 510 N, refresh rate 72 Hz) located 29 cm above the robotic arm such that images displayed on the monitor appeared to lie in the same horizontal plane as the robotic arm. A 43 cm (length) × 33 cm (width) × 0.30 cm (height) touchscreen panel (Keytec Inc., Garland, TX, USA), with a resolution of 4,096 × 4,096 pixels was horizontally mounted 2.5 cm above the robotic arm, more specifically the screw head where participants placed their thumb. This is used to record reach endpoints, made with the left hand, to proprioceptive hand-targets, the felt location of the right thumb resting on top of the robot handle, such that the thumb was just under the touchscreen. The lights were dimmed, and the subject's view of their training (right) arm was blocked by the reflective surface and a black cloth was draped over their right shoulder. The view of the untrained left hand was not concealed, and lit by a small lamp, so that the left arm was visible during the proprioceptive localization task, and any errors in reaching to the unseen right target hand could not be attributed to errors in localizing the left, reaching hand.

Visual Targets: The targets were located radially, 12 cm from the home position at 60°, 90° and 120° in polar coordinates, each represented by a 1 cm diameter yellow

circle (Fig 1B). Figure 1B-D displays the different tasks and target locations used throughout the experiment. The cursor, used to represent the subject's hand, was a green circle 1 cm in diameter. The home position was visible only briefly before the target onset and to guide participants back to the home position during two of the three tasks, it was located 20 cm in front of the subject at their body midline. The home position and the target were never shown at the same time. The intertrial interval, where participants' right adapted hand was locked at home, lasted 500 ms.

Proprioceptive Stimuli: For proprioceptive localizations, the right hand served as a target, and it was passively moved by the robot to one of the three target locations previously described. A beep then signaled for participants to use their left untrained hand to indicate on a touchscreen to the felt location of their trained right hand underneath the touchscreen (Fig 1D). Once the touchscreen registered their touch, the right target hand was allowed to move freely back to the home position along a robot-constrained path (c.f., Cressman & Henriques, 2009; 2010), while only the home position was visible. The hand was then locked at the home position for 500 ms before it was passively moved to the next target site.

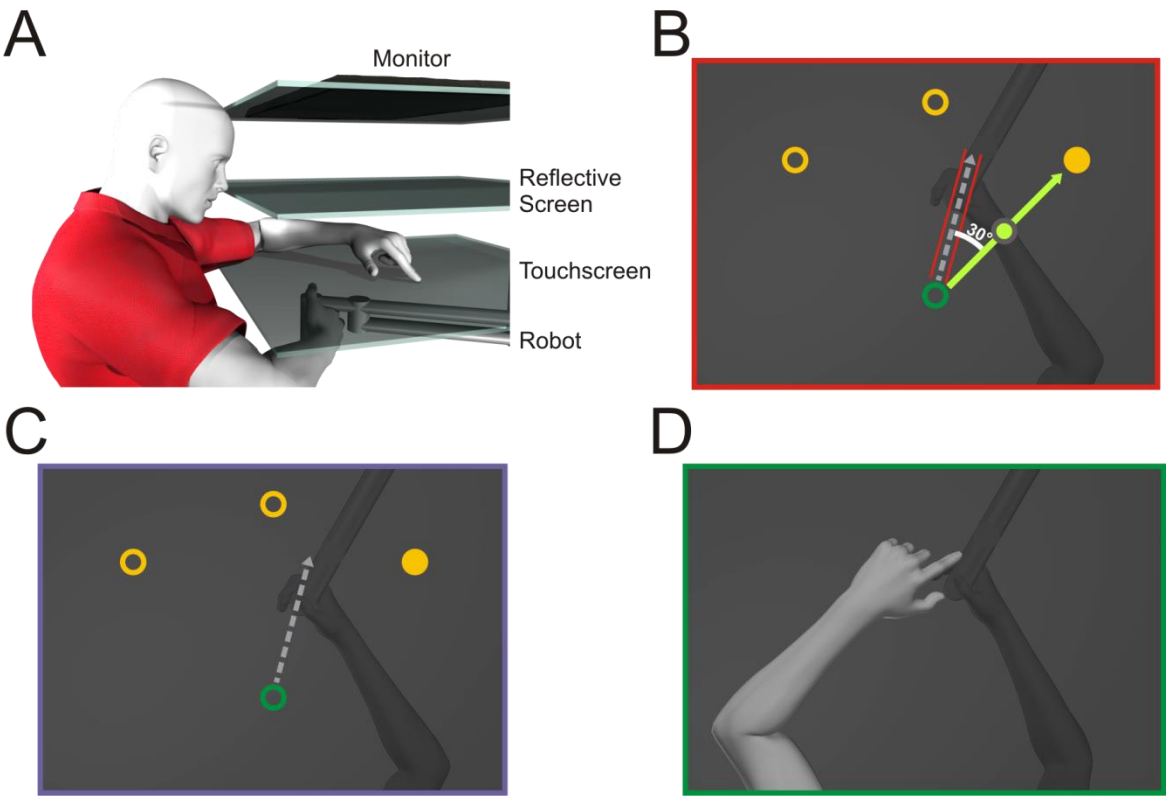

Fig 1. Experimental setup and design. **A:** Side view of the experimental set-up. The top layer is the monitor, middle layer is the reflective screen, and the bottom opaque layer is the touchscreen. The robot is depicted beneath with the participants' right hand grasping it. **B-D:** Top views of task specific set-ups. **B**: **Training task.** The home position is represented by a green circle with a 1 cm diameter; located approximately 20 cm in front of the subject and not visible during the trial. Targets are represented by yellow circles with a 1 cm diameter located 12 cm radially from the home position at 60°, 90° and 120°. The target was visible for 300 ms, after which it disappeared and participants moved their hand along a robot-constrained path (this force channel is shown in red) to its remembered distance. During rotated exposure training the participants' hand path (force channel) was rotated 30° CCW with respect to the start location. **C No-cursor reach task.** A target (same three as for the training task) would appear and stay visible; the participant would freely reach to its location, without robot restraint, but without the cursor or any other visual feedback of the hand. The trial ended when the hand held still for 250 ms. **D: Localization task.** In the proprioceptive localization task, the robot passively moved the unseen, right trained hand to one of the three target locations. The participants then used the index finger of their left untrained hand to indicate the felt location of the right hand (specifically the thumb).

General Procedure

To allow for direct comparison to a previous study using classic training, the procedures here match that of Ruttle et al., (2016) as much as possible. The experiment was comprised of an Aligned and Rotation condition, each of which consisted of a repeated series of three tasks (Fig 2). The Aligned condition was used to collect

baseline measures while training with a cursor whose motion was aligned with the hand movement. The Rotation condition abruptly introduced a 30° CW discrepancy between the direction of cursor motion and robot-generated hand path during training.

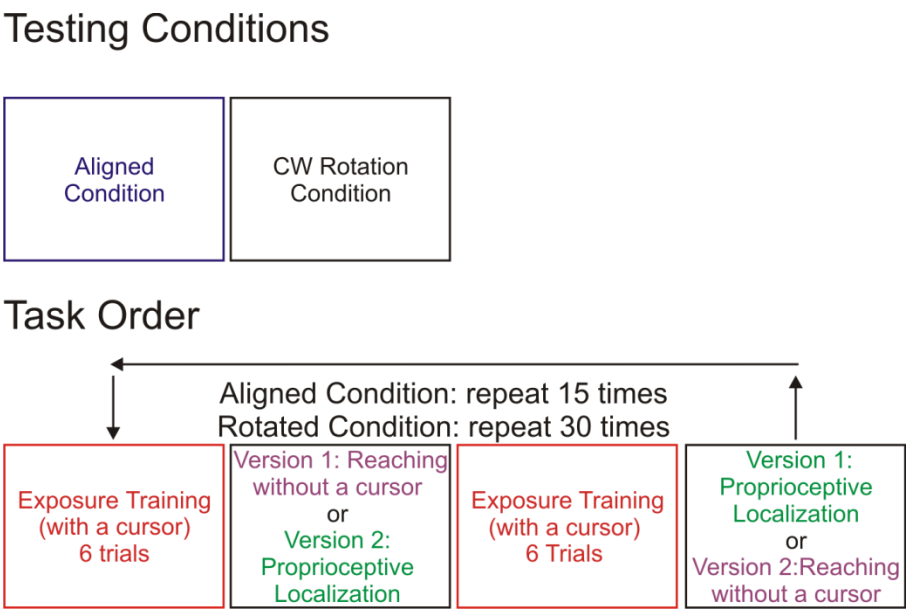

Fig 2 Testing Session breakdown. Participants completed three tasks under two separate conditions, that include exposure training with an aligned cursor and with a cursor rotated 30° CW. Participants completed a total of 270 (18 trials X 15 iterations) trials during the **aligned condition** and 540 (18 trials X 30 iterations) trials during the **CW rotation condition**. Each block of 18 trials included 12 training trials, 3 no-cursor trials and 3 localization trials. All participants completed the same tasks throughout training, but the order in which the tasks were completed was counterbalanced across participants with two versions of task order **(version 1 and version 2)**.

Exposure Training

Participants began each session with six exposure training trials (Fig 2 red box). Before each set of six trials the word “Cursor” appeared for 1000 ms to indicate the type of subsequent task. After this a target would appear for only 250 ms, and participants moved their hand along the robot-generated constrained path in order to move the cursor toward the target site. Unlike during traditional visuomotor rotation training, the robot only allowed participants to move their hand forward and back along a constrained pathway, this ensured the green cursor always went straight to the intended target. If

they attempted to move outside of the pathway, a resistant force, proportional to the depth of penetration with a stiffness of 2 N/mm and a viscous damping of 5 N/(mm/s), was created perpendicular to the pathway (c.f. Henriques & Soechting, 2003). Once the participant had moved at least 9 cm out and held their hand still for 250 ms, the green cursor turned red signaling the end of the trial. The hand returned along the same path by the robot at a speed of 4 cm/s and was held in the home position by the robot for 500 ms, when the next trial began. We will refer to this task as exposure training as participants don't decide their movement trajectory, and only determine how far their hand moved along the constrained path, while being *exposed* to a discrepancy between visual and proprioceptive feedback on their movement. This eliminates any possible visual sensorimotor error signals. For the aligned cursor exposure training, sets of 12 trials were repeated 15 times for a total of 180 trials. In the rotated cursor exposure training, these sets were repeated 30 times for a total of 360 trials.

In order to ensure participants were looking at the cursor during exposure training, as in our previous studies (Cressman & Henriques, 2010; Salomonczyk et al., 2013) we had the cursor blink on 50% of all trials for 33.3 ms, along the middle half of the cursor motion. At the end of the trial, participants reported if the cursor blinked or not by pressing one of two keys with their left hand. A single beep was given when participants gave the incorrect answer, e.g. saying it didn't blink when it did or vice versa. Participants were correct ~88% of the time, so all were included in the subsequent analysis.

Reaching without a cursor

Reaching without a cursor before and after training with a rotated cursor is common method for measuring reach aftereffects (Fig 2 purple box). But for this study, we wanted to measure the time course of these deviated movements, so we sampled every six trials throughout both training sessions. More specifically, after completing at least six exposure training trials participants completed three no-cursor reaches, one to each of the same three targets as during exposure reaching. This task is very different from the exposure training trials as the subject has full control over their movements and is not constrained in any way. The words “No-Cursor” were displayed for 1000 ms before each block of three trials. The participants were required to reach to the target, stop when they believed they had achieved the target, and hold their hand still for 250 ms to complete the trial; they received no feedback on how close their reach was to the target. At that time, the target disappeared and the home position appeared and participants returned to the home position just as in the exposure training task (along a robot-generated path). During aligned-cursor training (Fig 2 blue box), there were 15 iterations of 3-trials (45 no-cursor reach trials in total), while during the rotated-cursor training conditions (Fig 2 black box), there were 30 iterations (90 trials in total).

Proprioceptive Localization

The proprioceptive localization task differs from the previous two tasks in that there was no visual stimulus (no visible target; Fig 1D and Fig 2 green boxes). Participants were directed with the words “Reach to Hand” for 1000 ms before each block of three trials. During proprioceptive localizations the trained right hand was used as the target, which was moved by the robot to one of the three target locations. This passive movement of the hand took 650 ms to cover the 12 cm distance (see Cressman

& Henriques, 2009). A beep signaled participants to use their left index finger, on a horizontal touchscreen (Fig 1A and D), to indicate the felt location of the unseen right target-hand, more specifically the thumb. Once the touchscreen response was registered, the robot released the right target hand and the home position reappeared. During aligned cursor training (Fig 2 blue box), there were 15 iterations of 3-trials (45 proprioceptive localization trials in total), while during the rotated cursor training condition (Fig 2 black box) there were 30 iterations (90 trials in total).

We interleaved these three tasks to get a clear picture of the rate of sensory and motor changes which arise during repeated exposure to a visual-proprioceptive discrepancy. Exposure training was always the first task, but to counterbalance task order, half our participants completed three no-cursor trials immediately after the first set of training (version one), whereas the other half immediately completed three proprioceptive localizations (version two). All participants then completed six more training trials and then the other task than previously completed (Fig 2).

Proprioceptive localization calibration

At the end of the testing day, we had a final task for calibrating the touchscreen axes. Prior to this task an additional light was turned on so the right trained hand became visible, removing any proprioceptive recalibration. Here the robot guided the visible, right target hand to one of the 5 targets (30°, 60°, 90°, 120°, 150° and the home position) participants then reached with their left hand and indicated on the touchscreen the felt location of the visible right target hand. They are instructed to indicate on the touchscreen where they see their right thumb. They localized each target 5 times and

returned to the home position 5 times for a total of 30 calibration trials. The entire experiment took approximately 75 minutes to complete.

Data Analysis

The main goal of this study was to identify the time course of changes in reach aftereffects and proprioceptive recalibration when participants are exposed to a visual-proprioceptive discrepancy without making voluntary reaching movements. Given that participants did not make volitional reaching movements, but had their hand motion directionally constrained, we focused on reach errors during no-cursor reaches (reach aftereffects) to quantify motor learning, and changes in hand localization to measure proprioceptive recalibration. To measure the overall motor and sensory changes, we analyzed results across three sets of “Blocks”: each block or time point analyzed was an average of three trials. These averages came from the final aligned trials, the initial and the final rotated trials.

Reaching without a cursor

To determine if participants altered their reaches as a result of exposure training with the 30° CW rotation, we measured reach endpoint errors when receiving no visual feedback of hand location (no-cursor trials). The reaching error is calculated based on the angular deviation between the reach endpoint and the target location, relative to the home position.

Proprioceptive Localization

The analysis of proprioceptive changes was based on the angular endpoint error as provided by the difference between the movement endpoint and the responses on the touchscreen. We expected to see a similar size of shift in proprioception as in the reach aftereffects, which is why we also measured endpoint position for the no-cursor reaches.

Comparison to classic training

In addition, we wanted to compare the data collected in this study (n= 19) to those collected from a previous study with a very similar experimental paradigm (n = 20) (Ruttle et al., 2016). The training paradigm used in Ruttle, Cressman, 't Hart, & Henriques, (2016), allowed participants full control over hand movements. This made multiple error signals available for use in adaptation. In the current study, we used an exposure paradigm where the participants were not able to choose the direction of movement and thus received no error signal from movement discrepancy. Participants did not return to test retention, so they only learned one rotation. Apart from this the trial schedule was exactly the same, allowing comparison of the effect of the training types on no-cursor reach errors and proprioceptive estimates of hand location.

Power Analysis

To ensure we would find the effect we were looking for we completed an analysis of power to assess our sample size. The t-tests executed were all preplanned and thus we could use a conventional alpha of .05 which during our repeated measures within subjects designs allowed for power of .96, this was scaled down to .84 with a more conservative alpha of .01. We also completed a few Independent between subject's

comparisons that with an alpha of .05 allowed us to find an effect 77% of the time, but this was reduced further to only a 53% chance with an alpha of .01. These analyses were conducted assuming we only achieved a Cohen's D of .9 which we exceeded in many cases.

Analysis

Reach deviations, proprioceptive recalibration and the similarities across training types were analyzed using identical procedures. In order to assess the progression of change in aftereffect reaches and proprioception and how they differ across training we began with a Mixed-ANOVA that included three Blocks (aligned final, rotated initial and final) and an additional factor of training paradigm (classic vs. exposure) for both proprioceptive localizations and reaches without visual feedback (separately). The significant results of these multifactor ANOVAs are not reported for brevity, but instead the main planned comparisons (t-tests) necessary to test our hypotheses are reported. When performing the between subjects t-tests across the two experiments (for classic and exposure training), the results during the first and final block of rotated training were calculated with respect to the relevant baseline values (they were subtracted out) and these normalized values were compared across the groups. The t-tests comparing across blocks were a within subject design but the data was normalized for consistency. To counteract any family-wise error (inflation of Type 1 error), for pairwise analyses of the three blocks, we will use a stricter p-criterion of 0.01 rather than 0.05 (similar to Bonferroni correction).

Results

Reaching without a cursor

To gauge the effect of the cross-sensory error signal on the time course of motor changes, participants passively experienced exposure to a visual-proprioceptive discrepancy. This training resulted in no volitional reaching data when the cursor was visible. Reaches completed with the cursor are typically used to confirm participants were able to counter the imposed distortion. Without this we instead used subjects' no-cursor reaches to quantify motor change. Participants completed three no-cursor reaches every 12 training trials. They were fairly accurate when completing this task in the aligned condition, with a bias of 4.39° averaged across all 19 subjects. However, after training with the misaligned cursor subjects showed significantly deviated reach aftereffects compared to aligned training. The solid purple curve in figure 3A displays the time course of reach aftereffects across all the misaligned exposure trials (left panel). Only 6 or 12 visual-discrepancy trials were necessary to create significant changes in motor output with reach aftereffects of 5° [aligned vs. initial block: $t(18)=-3.544$, $p=.002$, $d=-1.14$]. These reach deviations continued to significantly increase following another 168 -174 training trials by 5.57° [initial vs. final: $t(18)=-3.806$, $p=.001$, $d=-1.22$]. Participants showed significantly deviated no-cursor reaches following exposure training with a small visual-proprioceptive discrepancy.

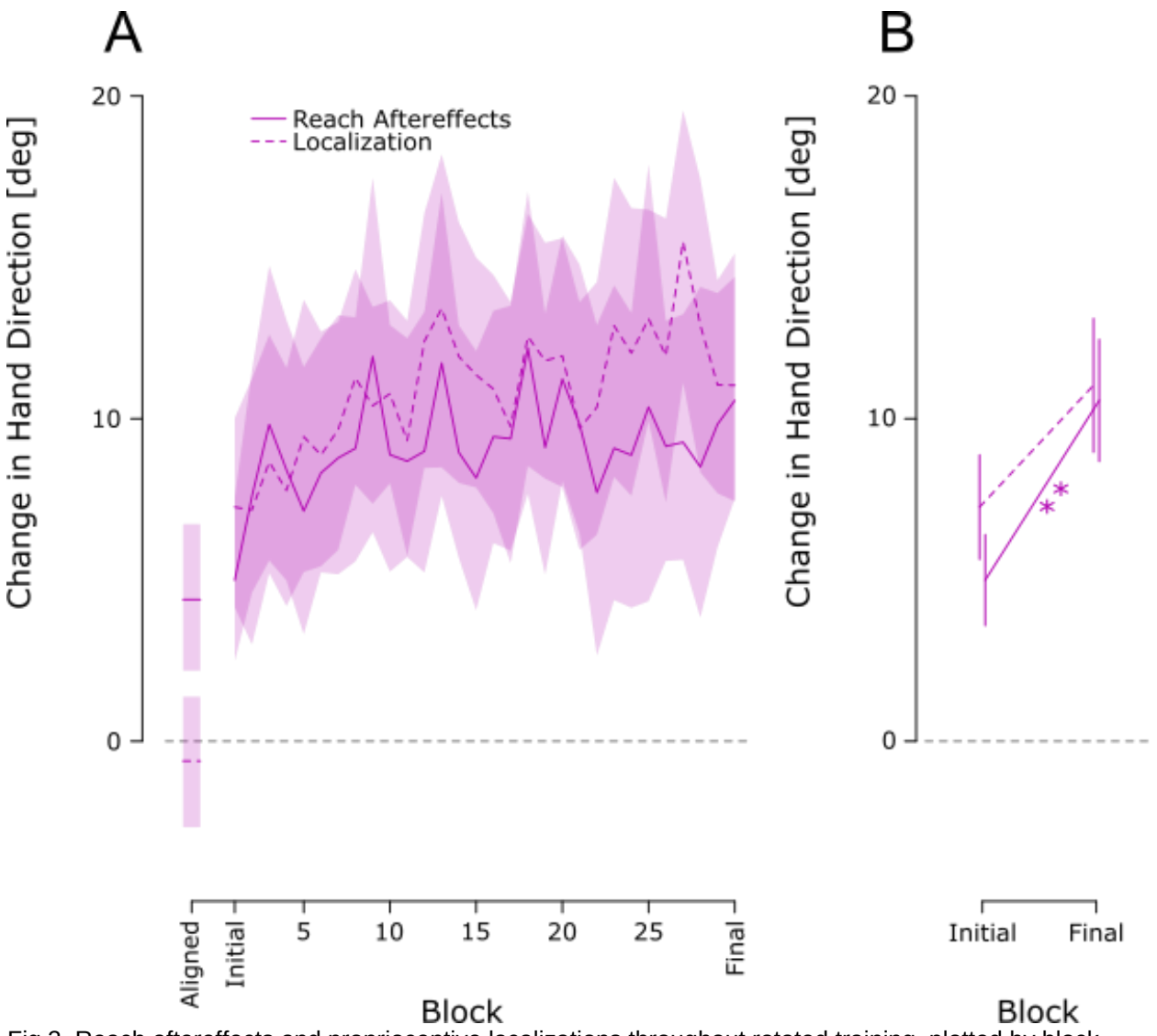

Fig 3. Reach aftereffects and proprioceptive localizations throughout rotated training, plotted by block. Mean change relative to baseline in angular endpoint error for both no-cursor reaches (solid line) and proprioceptive localizations (dotted line) during rotated training. The proprioceptive localizations have been flipped for ease of viewing. **Panel A:** The normalized data are plotted across blocks, each block an average of 3 trials, one to each target location. The lines within the coloured curves represent the block means while the coloured areas represent a 95% confidence interval. **Panel B:** Simplified view of panel A, the mean changes at each of the time points used for statistical analysis. The data shown here have been normalized by subtracting each participant's aligned bias from their performance during exposure training. The asterisk indicates significant differences between blocks; one star is significant to .01, two stars are significant to .001.

Proprioceptive Recalibration

Subjects were quite good at identifying the location of their unseen hand during veridical training, falling on average within a degree of the target site (.9°). But not

surprisingly they significantly shifted this felt estimate of the unseen hand following passive exposure to the cursor-hand discrepancy. The dotted purple curves in figure 3A illustrate this change in proprioceptive localization across the blocks of misaligned visual-proprioceptive exposure (left panel) and between initial and final block of exposure (right panel). When comparing the final aligned trials to the initial block of trials completed during this misaligned training subjects' felt hand position was already shifted by 7.5° [aligned vs. initial: $t(18)=4.4807$, $p<.001$, $d=1.44$]. This large shift continued to increase across the subsequent training trials to 11.32° but this was not significant [initial vs. final: $t(18)=2.421$, $p=.026$, $d=.78$]. In summary, a proprioceptive mismatch is enough to cause subjects to significantly shift their felt hand position with only six exposure trials.

Volitional Training vs. Exposure Training

An equally important goal of this study was to compare the learning curves for motor and proprioceptive changes that occur during classic and exposure visuomotor training. Classic being where the hand movement is generated by the participant and exposure when the hand is moved and deviated from the cursor motion by the robot. Both studies were carried out in the same lab, using identical experimental paradigms (Ruttle et al., 2016). The only differences were the subjects and the type of training each group experienced. All participants, regardless of training type, experienced an aligned condition prior to training with a 30° clockwise rotation. We first compared the time course of changes in no-cursor trials (reach aftereffects) across the two types of training. Figure 4A shows the classic learning curves in green with the reach aftereffects during exposure training shown in purple. Despite a significant difference in the direction

of no-cursor reaches produced during aligned-cursor training in both experiments (Aligned: $t(37)= -3.215$, $p=.002$, $d=-1.03$), the significant shift in these no-cursor reaches, i.e. the reach aftereffects, that emerged after the initial block (6-12 trials) of training did not significantly differ between the two types of training (Initial: $t(37)= -1.581$, $p=.119$, $d=-.51$). Participants who trained in the exposure condition had initial reach aftereffects of 5° and those in the volitional training groups reach aftereffects were 8°. Following an additional 324-330 training trials those who experienced exposure training exhibited reach aftereffects of 10.5°. As expected, those who experienced classic training had reach aftereffects much larger than the exposure training group which trended towards significance, 15.5° (Final: $t(37)=2.503$, $p=.015$, $d=.8$). These results suggest that large aftereffects need volitional training to be produced with exposure training leading to smaller but still significant motor changes.

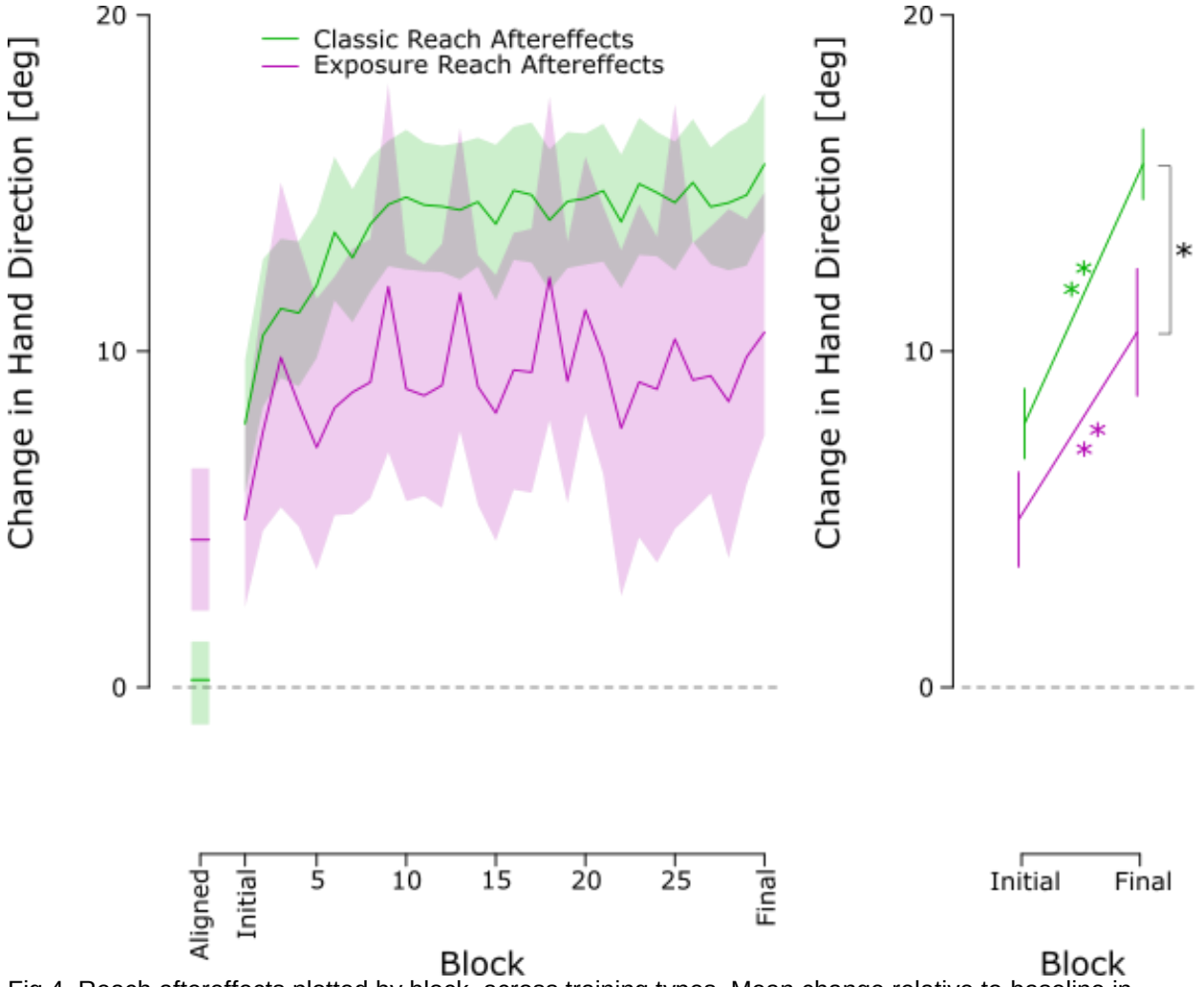

Fig 4. Reach aftereffects plotted by block, across training types. Mean change relative to baseline in angular endpoint error for classic (green) and exposure (purple) no-cursor reaches during rotated training. **Panel A:** The dark coloured curve represents aftereffects during and following classic visuomotor training; whereas the lighter curve represents the exposure training paradigm. The data are plotted by block, an average of 3 trials. The lines within the coloured curves represent the block means while the coloured areas represent a 95% confidence interval. **Panel B:** Simplified version of panel A, only includes the mean change at each time point used for statistical analysis. The data shown here have been normalized by subtracting each participant's aligned bias from their performance during exposure training. The filled in circles represent classic visuomotor training and open circles represent the exposure training paradigm. The asterisk indicates significant differences between blocks; one star is significant to .01, two stars to .001.

Proprioceptive localizations were fairly similar in their pattern of change across training types (green curves in figure 5). Both groups were very accurate when localizing their hands during aligned training (exposure training .90°, classic training .32°, t(37)= -1.934, p=.058, d=-.62). After the first block of training, 6-12 rotated training trials, both groups of subjects had equivalent shifts in felt hand position (Initial:

t(37)=1.609, p=.113, d=.52), those in exposure training shifted 7.6° and volitional training caused a shift of 4.2°. By the final block of training the two groups of participants had begun to differ (Final: t(37)=2.910, p=.005, d=.93). Those in the exposure training group had shifted their felt hand position by 11.3° whereas those in the volitional training group had only shifted by 5.09°. In conclusion, it appears that visual-proprioceptive exposure training can produce a much larger shift in felt hand position than volitional visuomotor training.

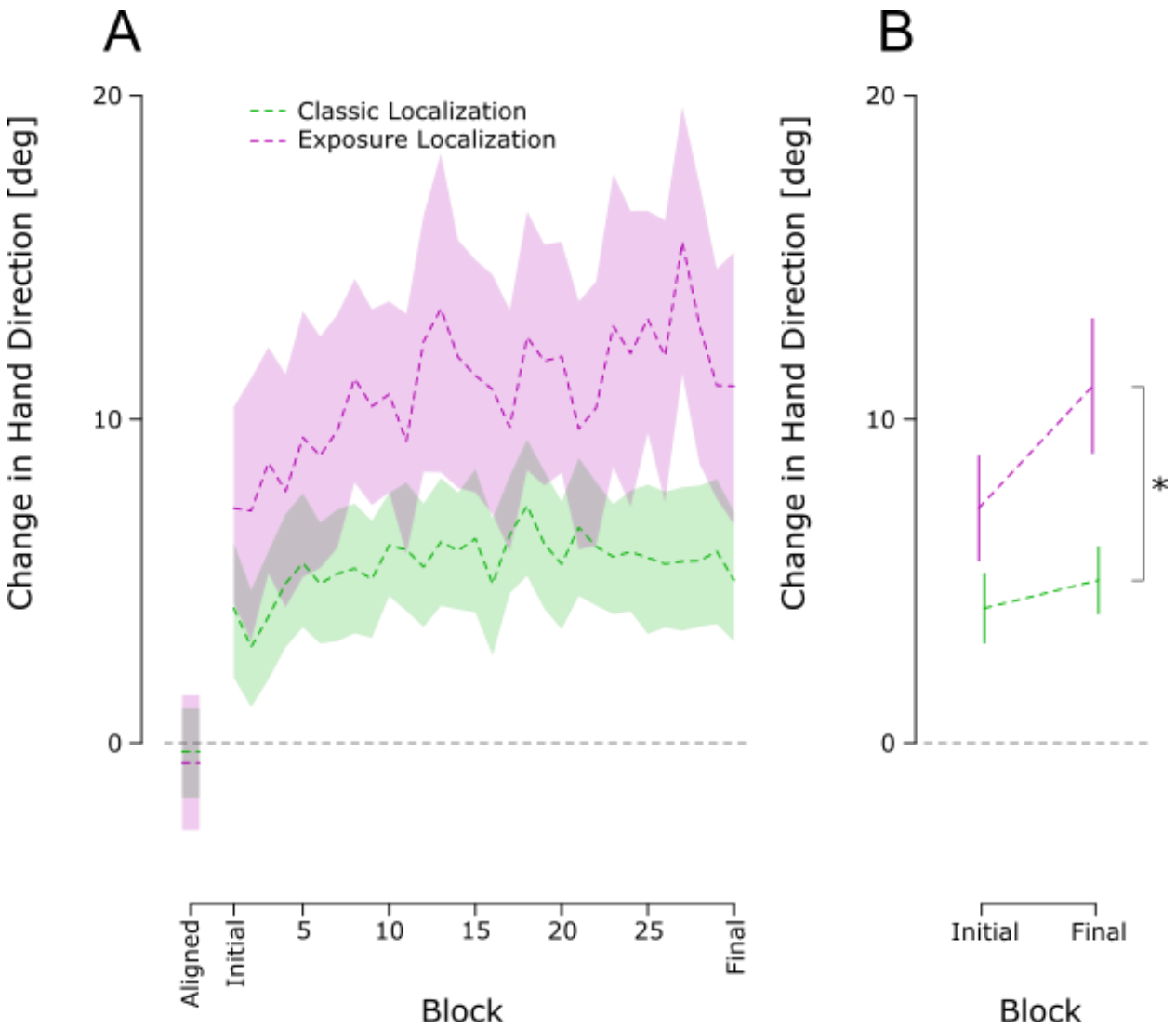

Fig 5. Changes in proprioceptive localizations across training types. Mean change relative to baseline in angular endpoint error for classic (green) and exposure (purple) proprioceptive localizations during rotated exposure training. **Panel A:** The dark coloured curve represents classic visuomotor training, whereas the lighter curve represents the exposure training paradigm. The data are plotted by block, an average of 3 trials. The lines within the coloured curves represent the block means while the coloured areas represent a 95% confidence interval. **Panel B:** Simplified version of panel A, only includes the mean change at each time point used for statistical analysis. The data shown here have been normalized by subtracting each participant's aligned bias from their performance during exposure training. The filled in circles represent classic visuomotor training and open circles represent the exposure training paradigm. The black asterisk indicates a significant difference between the blocks; one star is significant to .01.

Discussion

Here we have shown that exposure to a discrepancy between seen and felt hand location (exposure training) is sufficient to cause motor adaptation rapidly. The rate appears to be similar to classic visuomotor adaptation training, where the sensory discrepancy is accompanied by self-generated movements. Not only did reach aftereffects and proprioceptive localizations develop equally fast, they were already significantly deviated after just 6 training trials. When comparing across training types we found reach aftereffects to be larger following classic training than exposure training. We also find a difference in the extent of proprioceptive recalibration across training types. In summary, it appears the proprioceptive-visual discrepancy is sufficient to evoke sensorimotor adaptation as quickly as classic training but without additional error signals and in absence of self-generated movements.

Time Course of Classic Visuomotor Adaptation

The time course of classic visuomotor adaptation is consistently found to be quick with initial learning taking very few trials to return to baseline, usually within 20 trials for a 30° rotation (Krakauer et al., 2000). Some researchers have attributed the shape of this time course (decrease in errors) as reflecting two separate systems that

drive motor adaptation, a fast and a slow system (Smith et al., 2006). The fast system responds strongly to errors, contributing to quick changes in hand movements during the initial rotated-cursor training trials. Compared to the fast system, the slow system is less sensitive to error, proceeds more gradually and persists for a longer period. The task used here made it impossible to fit this model so we are not able to comment on the role aftereffects or proprioceptive recalibrations play in the model. For now the part motor and sensory changes play in the multi-rate model is unknown.

Very few studies have investigated the progression of sensory and motor changes during classic visuomotor adaptation. This is important for understanding each sensory signals individual contribution and may reveal insights into possible underlying mechanisms. Mattar, Darainy, and Ostry, (2013) collected estimates of felt hand movement direction intermittently during force field training to identify the time course of somatosensory changes. They found that felt estimates of hand direction took ~76 trials to become significantly shifted from baseline. This finding was also found by Zbib, Henriques, and Cressman, (2016) for a visuomotor rotation paradigm, where it took over 70 trials for a significant shift in proprioceptive estimates to occur. However, the rather slow somatosensory changes may partly have to do with the method used to estimate these changes. That is, the two-alternative choice method employed by (Mattar et al., 2013; Zbib et al., 2016) required a minimum of 50 trials to measure a somatosensory estimate of hand direction at one location. However, with a quicker method for measuring proprioception, we previously found that proprioceptive changes already plateau after just six trials (Ruttle et al., 2016). Zbib et al., (2016) measured reach aftereffects both before and after each set of proprioceptive estimate

measurements and found a significant amount of decay between those two time points. This may have also influenced the speed of overall learning and thus proprioceptive recalibration. With our faster method, we found that there was significant proprioceptive recalibration after only 6-12 trials of visuomotor rotation training (Ruttle et al., 2016). Moreover, in the current study we found the same was true even when training did not involve self-generated movement as in classic visuomotor adaptation. This suggests that these somatosensory changes are not only robust but are quite sensitive to visual discrepancies as illustrated by this rapid shift in both types of training. These results also suggest that the mechanisms underlying proprioceptive recalibration may be different from those producing changes in movement.

Mattar et al., (2013) did not measure reach aftereffects until the very end of training and therefore was unable to comment on the time course of motor changes. However, Zbib et al., (2016) measured aftereffects and found that only five rotated training trials were required to create a significant shift in reach direction, there was no additional increase after ~40 training trials. Ruttle et al., (2016) measured reach aftereffects every six rotated training trials and the resulting speed of motor changes was very similar to Zbib et al., (2016). Participants required only six rotated training trials before exhibiting significant reach aftereffects (Ruttle et al., 2016). In the current study we find the same time course in motor changes found by Ruttle et al., (2016) and Zbib et al., (2016) even though the motor system was not fully engaged in exposure training. Likewise, the size of reach aftereffects plateauing at approximately the same time (~40th trial) as those found in Zbib et al., (2016). This plateau in aftereffects has been seen in many studies that include prolonged training (Salomonczyk et al., 2011;

Wong & Henriques, 2009; Zbib et al., 2016). Reach aftereffects evolve and plateau quickly in a way that resembles the time course produced during rotated-cursor reaches (i.e reach training) but seems to differ slightly from that of proprioceptive recalibration.

Exposure/Passive Learning

To be able to identify the role proprioception and its related error signals play in motor adaptation we employed a paradigm designed in our lab that only provides a visual-proprioceptive mismatch. Our original paper (Cressman & Henriques, 2010) showed that proprioceptive recalibration was equivalent to that seen following classic training (Cressman & Henriques, 2009) and that this training led to significant reach aftereffects. These exposure-driven reach aftereffects were smaller than those produced during classic visuomotor training; they instead were closer in size to that of proprioceptive recalibration. Exposure training to different sizes of visual-proprioceptive discrepancies also leads to similar motor and sensory changes which do not increase with the size of the discrepancy (Salomonczyk et al., 2013). Changes in open-loop movements and hand perception were also found by Cameron, Franks, Inglis, and Chua, (2012) where participants experienced both classic and exposure training, to a visual misalignment that resembled more of a change in gain rather than rotation, and exhibited near equivalent changes in felt hand position and aftereffects.

These training types have been used with patients to help identify possible brain areas associated with each signal. Henriques, Filippopulos, Straube, and Eggert, (2014) tested healthy older adults and mild cerebellar ataxic patients on both types of training and found similar shifts in proprioception, as well as smaller reach aftereffects following

exposure training than classic, for both groups. These results suggest that the cerebellum is not required for proprioceptive recalibration and thus must be occurring in another brain area, such as the posterior parietal cortex (PPC) (Della-maggiore, Malfait, Ostry, & Paus, 2004; Henriques et al., 2014; Shadmehr, Smith, & Krakauer, 2010). The PPC has been shown to be involved in state estimation (Buneo & Andersen, 2006; Shi & Buneo, 2011), as it receives multisensory information, making it a likely candidate for involvement in proprioceptive recalibration. This is consistent with our working hypothesis that proprioceptive recalibration is likely due to mechanisms (and brain areas) that differ from those involved in motor recalibration and reach aftereffects which tend to depend more on the cerebellum.

But all these exposure training paradigms described above were introduced gradually and none measured proprioceptive recalibration or aftereffects more than once and usually only at the end of training. Sakamoto and Kondo, (2015) did have a variation of this passive training but always before or following classic visuomotor reach adaptation with a rotated cursor to test for transfer or interference. For instance, they found that experience of a visual-proprioceptive discrepancy (exposure training) facilitated training in a classic learning paradigm. The focus of the present paper was on the time course of sensory and motor changes and we wanted to be able to compare it to our previous study on this topic. For these reasons we chose to use an abruptly rotated cursor.

Here we found that despite no movement and thus no efference copy of intended movement, reach aftereffects were significant incredibly quick. Aftereffects similar to those found here have also been measured during gradual exposure training (Cameron

et al., 2012; Cressman & Henriques, 2010; Henriques et al., 2014; Salomonczyk et al., 2013). Interestingly, this passive exposure to a visual-proprioceptive mismatch also caused significant reach aftereffects of about 16-30% of the distortion. However, the reach aftereffects produced after exposure training were not as large as those following classic training (Cameron et al., 2012; Henriques et al., 2014; Salomonczyk et al., 2013). The current study supports this finding as there was a significant difference in reach aftereffects between classic and exposure training. Salomonczyk et al., (2013) also found that reach aftereffects grew with increases to the size of the distortion from 30° - 70° for classic visuomotor rotation training. But, they found no substantial increase in aftereffects past those created by the 30° distortion following similar increases in misalignment during exposure training. It would appear that larger and proportionally increasing reach aftereffects seen following classic training require experience with active movements. As well, it seems that aftereffects are not purely motor and perhaps as much as 60% are generated by the cross-sensory error signal.

As stated above most previous exposure training paradigms have used a gradually introduced perturbation and did not investigate proprioceptive changes throughout training. However, all those studies found similar changes in the extent of proprioceptive recalibration as we do here (Cameron et al., 2012; Cressman & Henriques, 2010; Henriques et al., 2014; Salomonczyk et al., 2013). Furthermore, these studies found proprioception recalibrated to a similar extent as during classic training, ~16-41% of the distortion. It is not surprising that proprioceptive recalibration still occurs and is similar to the change seen in classic training, if proprioception is responsible for some motor learning. Salomonczyk et al., (2013) gradually increased the size of the

distortion until it reached 70°. When participants experienced classic training, proprioceptive estimates continued to shift with the increase in distortion, but in exposure training proprioception did not significantly shift past 5.3°. In contrast to these studies we found a significant difference between proprioceptive recalibration following classic and exposure training (5.09° vs. 11.3°). This may be due to the method of proprioceptive measurement, proprioceptive-guided reaches compared to 2-AFC or possibly even difference in how quickly the misalignment was introduced. Because exposure training doesn't involve volitional movements during training, the usual motor-related error signals are reduced. Instead the only signal that remains to produce proprioceptive recalibration and reach aftereffect is the cross-sensory error signal, the mismatch between vision and proprioception. It is likely this common signal that leads to proprioceptive recalibration in both types of training, and moreover again contributes partly to the resulting reach aftereffects. That is, reach aftereffects following classical visuomotor adaptation is not purely motor-related. This suggests that proprioceptive plasticity in turn contributes to motor learning.

Conclusion

We abruptly introduced a proprioceptive-visual mismatch, and found similar learning extents as those seen with exposure to a gradual sensory misalignment, as seen in our other papers. This suggests that the cross-sensory error signal plays a large role in motor adaptation, evidenced by reach aftereffects immediately after 6 or 12 training trials, despite no active movements. The speed with which sensory changes occur, allow for proprioception to play a more leading role in motor learning than

previously assumed. To fully understand motor learning and the mechanisms involved, proprioception should be included in theories and models of motor learning.

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Supplementary Material

A: Gradual Data

Prior to the current study, our lab had only used the exposure paradigm with a gradually introduced cursor rotation (Cressman & Henriques, 2010; Henriques et al., 2014; Salomonczyk et al., 2013). Exposure training is produced by rotating the robot-constrained hand path (a force channel) away from the path the cursor moves, which is always straight to the target, and in this case, gradually. In an identical way to the abrupt exposure training described in the main thesis, the nature of this training removes any volitional hand movements and thus no efference copy of intended hand movements can be generated. As described above, this type of passive exposure training does consistently lead to significant changes in both felt hand position as well as reach aftereffects after a large amount of training (Cameron et al., 2012; Cressman & Henriques, 2010; Henriques et al., 2014; Salomonczyk et al., 2013). But since no one has ever tested an abrupt version of the exposure training, we were not sure whether we would see changes in either reach aftereffects or proprioceptive localization. Thus, we included both rotation schedules in the original experiment (nabrupt = 19, ngradual = 20) but given that reach aftereffects and proprioceptive recalibration arose even during abrupt-exposure training, the gradual version was no longer necessary. The abrupt-version of the exposure training is a better design for the goal of this study which was to measure the time course of these sensory and motor changes, and compare them with the changes from our published work using the classic abrupt visuomotor rotation training. Thus, we decided to only discuss the results of the abrupt experiment in the main thesis above. But for completeness, we briefly describe the gradual version of the experiment and the results here. The methods and task order were the same between

the two exposure experiments, with the only difference being the gradual cursor rotation which was introduced 1° at a time until at the full 30° rotation after 30 trials. Here I will outline the results of the time course of changes in reach aftereffects and proprioceptive localizations during and following exposure training using a gradual cursor rotation.

Reaching without a Cursor Results

Just as described in the main results section, participants did not create volitional hand movements during training, so the only way to assess the change, and more specifically the rate of change, was to measure volitional reaches without visual feedback of the cursor (no-cursor reaches) frequently throughout training. The solid line in Figure 5 display these reaches averaged across all subjects (solid line) plotted across either (A) all training blocks, including the last block during aligned training or (B) a subsets of these normalized blocks. As indicated by the first point of the Figure 5A, participants were fairly accurate when completing this no-cursor task in the aligned condition, with a bias of 1.51° when averaged across all subjects. However, after training with the misaligned cursor participants showed significantly deviated no-cursor reaches compared to those during aligned training. Upon further analyses it was clear that only 6 or 12 exposure training trials was sufficient to create significant changes in motor output [aligned vs. initial block: $t(19)= -2.82$, $p=.010$,$d= -.9$]. This is surprising given that at this point, these participants have only experienced a 6° to 12° rotation, but are already showing reach aftereffects or ~3°. These reach deviations continued to increase throughout training by 5.28° but this was not significant [Initial vs. midpoint: $t(19)= -2.507$, $p=.021$,$d= -.8$]. Following an additional 324-330 rotated training trials reach aftereffects only marginally increased and this was also not significant [midpoint

vs. final: t(19)= -.707, p=.488, d=-.23]. The size of the final change in reach aftereffects are similar to those found in previous studies, where reach aftereffects were measured only after extended training. This confirmed our expectations that a gradual exposure paradigm would create significant reach aftereffects. Moreover, these results also indicate that reach aftereffects can occur very quickly in response to a small visual-proprioceptive discrepancy in this passive training.

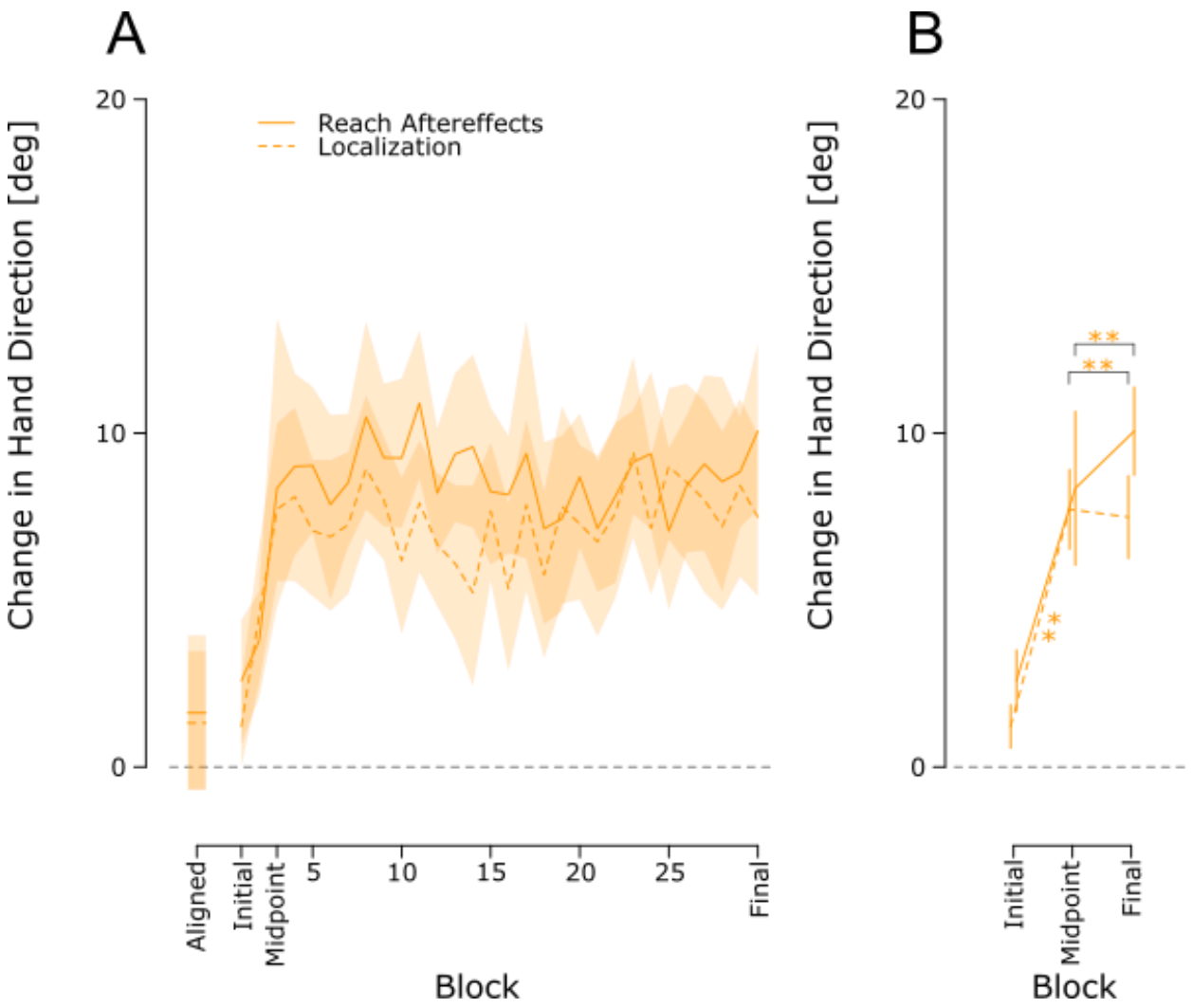

Fig 6. Gradual Exposure Training Reach Aftereffects and Proprioceptive Localizations. Mean change relative to baseline in angular endpoint error for both no-cursor reaches (solid line) and proprioceptive localizations (dotted line) during rotated-exposure training. The proprioceptive localizations have been flipped for ease of viewing. **Panel A:** The normalized data are plotted across blocks, each block an

average of 3 trials, one to each target location. The lines within the coloured curves represent the block means while the coloured areas represent a 95% confidence interval. **Panel B:** Simplified version of panel A, only includes the mean change at each time point used for statistical analysis. The data shown here have been normalized by subtracting each participant's aligned bias from their performance during exposure training. The asterisk indicate significant differences between blocks; one star is significant to .01, two stars to .001.

Proprioceptive Recalibration

Participants were quite good at identifying the location of their unseen hand during veridical training, being on average less than 2° away from the target (-1.32°) as plotted in the first block of Figure 5. The dotted curves in figure 5 illustrate the endpoint errors across all blocks (A) or a subset of blocks (B) for proprioceptive localizations once the visual-proprioceptive discrepancy was introduced. As we expected to see, exposure training with a gradually rotated cursor created significant shifts in felt hand position both during and following training. However, since the rotation did not acquire its maximum size until the 30th trial (or block 10), there was no significant shift in proprioceptive localizations [aligned vs. initial: $t(19)= 1.883$, $p=.075$, $d=.6$] following the first block of only 6-12 rotated trials (where the maximum rotation would have been 6° to 12°). However, by the midpoint block, when participants had experienced at least 1 full rotation trial, there was a significant shift in hand position of 8.96° [initial vs. midpoint: $t(19)= -6.113$, $p<.001$, $d=-1.96$]. There was no substantial increase in localizations following additional training [midpoint vs. final: $t(19)= -.199$, $p=.843$, $d=-.06$]. These results confirm that proprioceptive recalibration can occur without volitional hand movements.

Abrupt vs. Gradual Comparison

In this section, we will briefly compare the above results for sensory and motor changes across abrupt and gradual discrepancy introductions within the exposure experiment. When the participants aligned biases are accounted for there is no difference in the size of reach aftereffects exhibited after only 6-12 training trials [Initial: $t(37)=1.649$, $p=.107$, $d=.53$]. Once the gradually introduced discrepancy was at its maximum by the 30th training trials (we call here midpoint), reach aftereffects were still equivalent across training types [midpoint: $t(37)=.434$, $p=.667$, $d=.14$]. At the completion of training reach aftereffects following both rotation introduction types were similarly shifted, with an abrupt cursor rotation causing slightly larger reach aftereffects, but this difference was not significant [final: $t(37)=.221$, $P=.827$,$d=.07$]. In summary, there is no difference in reach aftereffects between abrupt and gradual rotation introductions when the participant experiences exposure training.

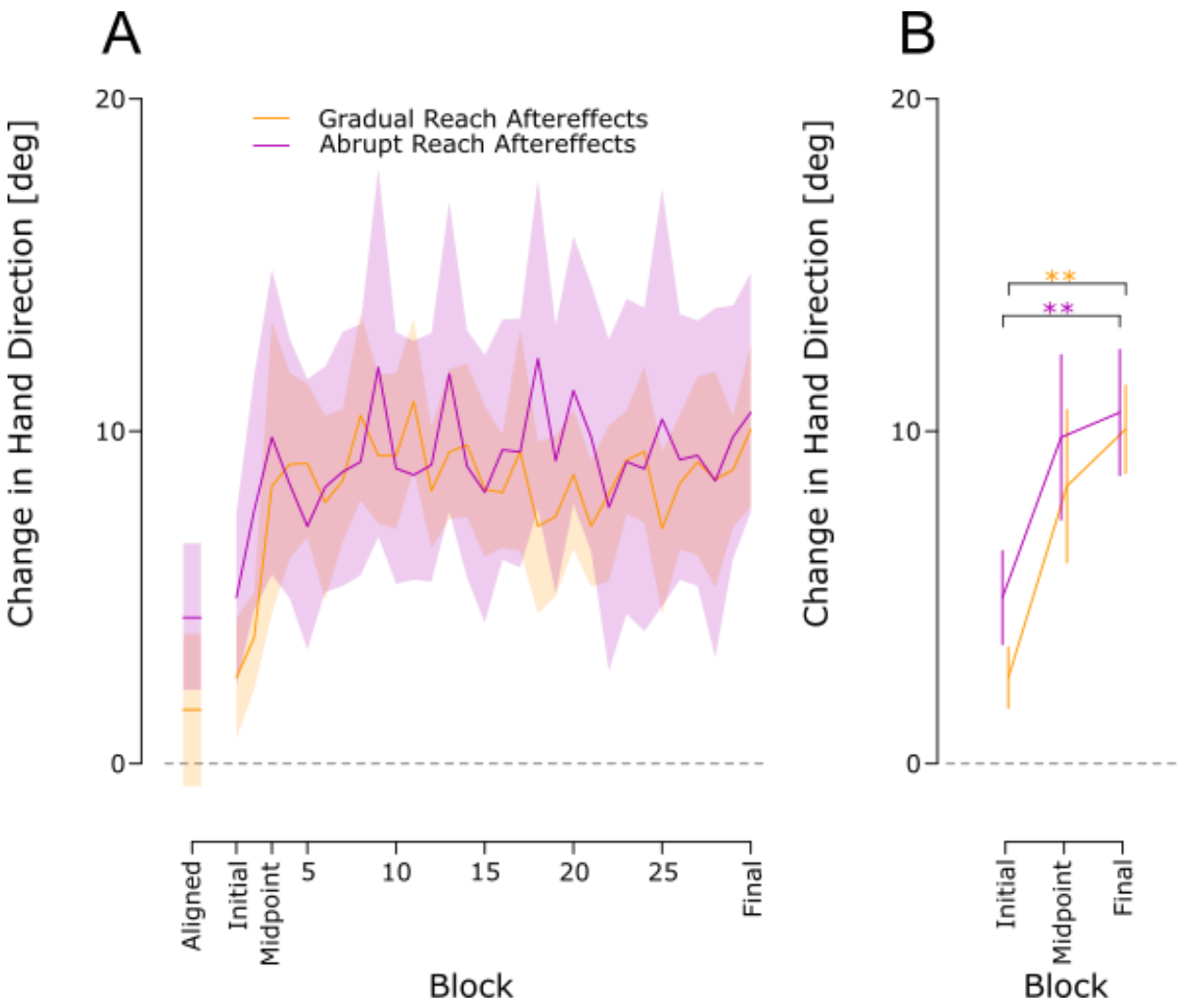

Fig 7. Abrupt and Gradual Reach Aftereffects. Mean change relative to baseline in angular endpoint error for both gradual (orange) and abrupt (purple) no-cursor reaches during rotated-exposure training. **Panel A:** The normalized data are plotted across blocks, each block an average of 3 trials, one to each target location. The lines within the coloured curves represent the block means while the coloured areas represent a 95% confidence interval. **Panel B:** Simplified version of panel A, only includes the mean change at each time point used for statistical analysis. The data shown here have been normalized by subtracting each participant's aligned bias from their performance during exposure training. The asterisk indicate significant differences between blocks; one star is significant to .01, two stars to .001.

In contrast to the reach aftereffects, there was a difference in the size of shift in felt hand position after the initial two blocks of rotated cursor training [initial: t(37)=-3.531, p=.001, d=-1.13]. By the midpoint, the felt hand position for both groups had shifted to the same degree [midpoint: t(37)=1.486, p=.146, d=.48]. After an additional

324 – 330 rotated training trials proprioceptive recalibration was still similar across rotation introduction conditions [final: t(37)=-.425, p=.674, d=-.14]. Regardless of the speed of the rotations introduction during exposure training proprioceptive recalibration occurs to a similar degree.

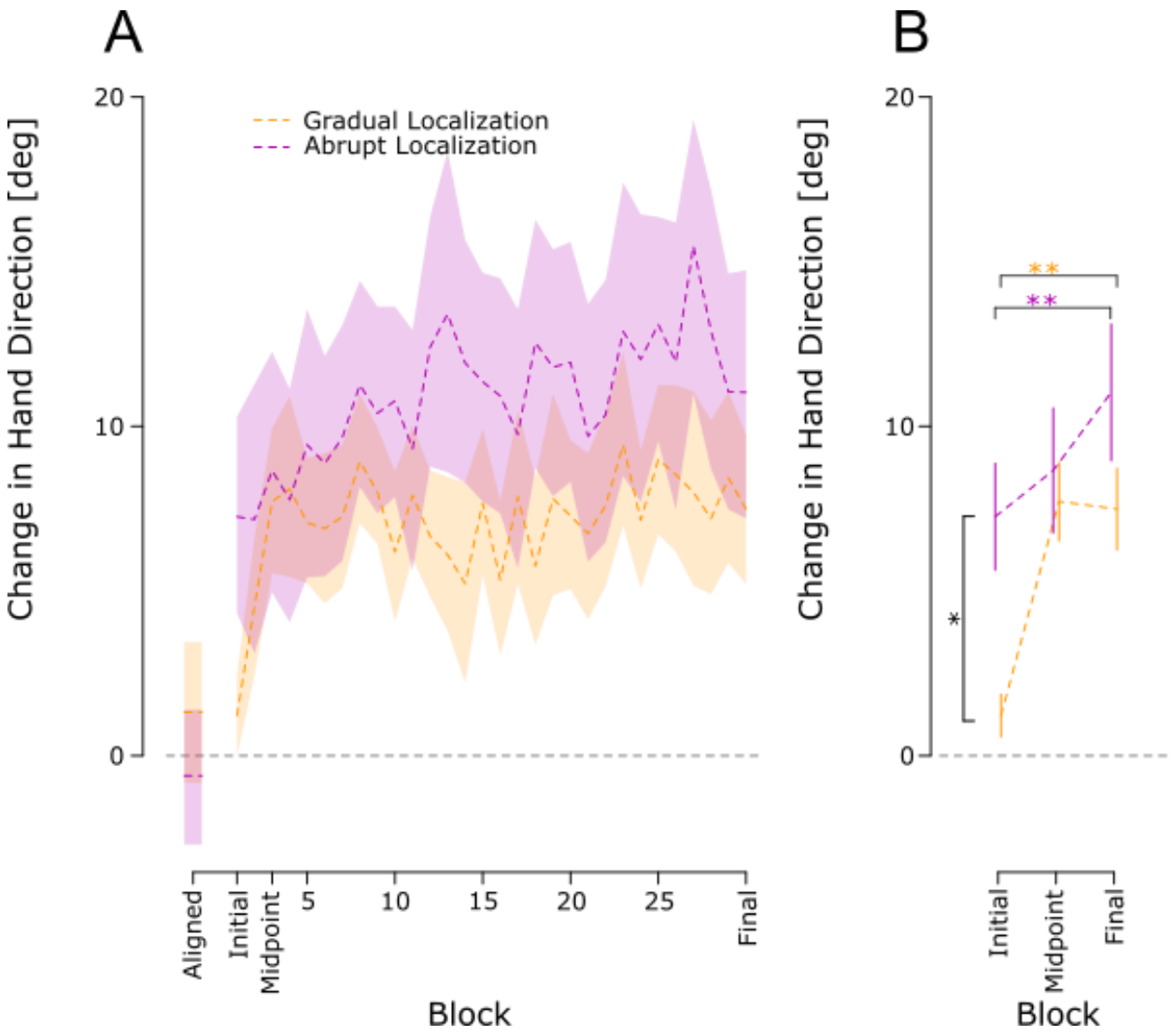

Fig 8. Abrupt and Gradual Proprioceptive Localizations. Mean change relative to baseline in angular endpoint error for gradual (orange) and abrupt (purple) proprioceptive localizations during rotated-exposure training. **Panel A:** The normalized data are plotted across blocks, each block an average of 3 trials, one to each target location. The lines within the coloured curves represent the block means while the coloured areas represent a 95% confidence interval. **Panel B:** Simplified version of panel A, only includes the mean change at each time point used for statistical analysis. The data shown here have been normalized by subtracting each participant's aligned bias from their performance during exposure

training. The asterisk indicate significant differences between blocks; one star is significant to .05, two stars to .001.

Conclusion

Our concern that we may find differences between gradually and abrupt introduction of the visual-proprioceptive discrepancy during exposure is based on some results for classic visuomotor rotation training that compared these two ways of introducing cursor rotation. A few labs believe gradual training leads to more complete learning and larger aftereffects, although this was for larger rotations of 60°-90° (Kagerer et al., 1997; Saijo & Gomi, 2010). But many other studies have found no such differences for small perturbations (Criscimagna-Hemminger et al., 2010; Schlerf et al., 2012; Venkatakrishnan et al., 2011; Werner et al., 2014). Likewise, when we compare across our own studies using gradual versus abrupt visuomotor rotations (Salomonczyk et al., 2011, 2012), we don't notice any differences in the size of the reach aftereffects nor the extent of the proprioceptive recalibration. Here we also found no difference in size of aftereffects or proprioceptive localizations following either training introduction. In fact, it appears as though abrupt cursor rotation training produced larger aftereffects and localizations than a gradual rotation. This confirms these earlier studies (Criscimagna-Hemminger et al., 2010; Venkatakrishnan et al., 2011) but may also be attributable to the different training paradigm used, no volitional hand movements. Exposure training may rely on the cross-sensory error signal which originates in a visual-proprioceptive mismatch. This may be a more consistent signal than the sensorimotor error signal and may produce similar learning across different paradigms.

B: Previous paper – referred to throughout (Ruttle et al., 2016).

Will add this before final submission.